

A second aspect of the invention provides a method of treating a patient undergoing vitamin D therapy for ESRD wherein a zero-intercept regression model is used to determine the initial dose of the vitamin D compound.

## 5     **Brief Description of the Drawings**

Figure 1 shows the observed dose vs. baseline PTH (dashed line) and the predicted dose vs. baseline PTH (solid line).

Figure 2 shows the difference in the observed dose and the predicted dose vs. baseline PTH.

10

## **Detailed Description**

As used in the specification, the following terms have the meanings indicated:

The term “**vitamin D compound**” shall refer to any vitamin D compound, including, an analog, derivative, or active metabolite thereof.

15

The term “**baseline PTH value**” or “bPTH” shall refer to the patient PTH value at the commencement of treatment with the vitamin D compound.

The term “**final dose**” shall refer to the final dose (in micrograms) of a vitamin D compound that is associated with the first stabile, clinically significant reduction in patient PTH values as determined for the vitamin D compound.

20

The term “**initial dose**” shall refer to the dose in micrograms that is the first or starting dose of the vitamin D compound administered to the patient as the patient commences treatment for secondary hyperparathyroidism and/or renal osteodystrophy. Initial dose is equal to the baseline PTH divided by a denominator based upon the outcome of a regression model.

09978853-101201

The present invention can be utilized to determine the starting dose of a vitamin D compound when used for the treatment of secondary hyperparathyroidism and/or renal osteodystrophy. Thus, the present invention is suitable for use in determining the initial dose of various vitamin D compounds currently approved for administration into humans, e.g., paricalcitol, calcitriol and doxercalciferol. Most preferred is the use of the present invention in determining the initial dose of paricalcitol.

Once the initial dose is determined for a vitamin D compound, the initial dose can be administered to a patient commencing treatment for renal osteodystrophy and/or secondary hyperparathyroidism with the vitamin D compound. The method described herein can be utilized in the treatment of these conditions regardless of the route of administration of the vitamin D compound. Preferably, when the vitamin D compound is administered according to the method of the invention, the administration is either oral or by injection, more preferably by intravenous injection.

We have determined that the initial dosing of vitamin D compounds can be based on patient baseline PTH while maintaining a safety profile consistent with approved dosing protocols, with no difference in the incidence of hypercalcemia. The method of the present invention utilizes regression analysis, preferably a zero-intercept linear model, to calculate an initial dose for the vitamin D compound. The data used in the model can be derived from a retrospective study of existing data. For example, the initial dose of paricalcitol has been determined from a retrospective study of clinical data. Thus, as long as sufficient dosing data is available to conduct the statistical analysis for a vitamin D compound, the method of the invention can be used to determine the initial dose for any vitamin D compound.

Once the model is in place, the predictability of the model can be verified by comparing the PTH values predicted by the model versus actual PTH values.

The determination of the initial dose is accomplished as follows. As a first step the patient's **baseline PTH** value is determined prior to the commencement of treatment with the vitamin D compound. Generally, patients having PTH values greater than 200 picograms per milliliter are considered to be candidates for vitamin D therapy. The determination of PTH values, including baseline PTH, is accomplished using methods that are well known in the art.

In addition to baseline PTH, the **final dose** must also be determined. Final dose is the amount of vitamin D compound that was administered prior to the first determination of a stabile, clinically significant reduction in PTH values. In practice, the vitamin D compound is administered and PTH values are monitored, generally at least weekly, until such time as the patient's PTH values have been lowered by a clinically significant value and remain stabile at that value. A clinically significant reduction, typically reported as a percent reduction from baseline PTH, is that percent reduction which has been determined to be of clinical significance. The clinical significance of a percent reduction is generally determined in a clinical trial of efficacy for the vitamin D compound and thus can range from about thirty percent to about sixty percent. In the preferred method of the invention, a clinically significant reduction is achieved with a thirty percent reduction in baseline PTH values. In addition to a clinically significant reduction in baseline PTH, the PTH reduction must be stabile for a period of time. The stability of the reduction must also be experimentally determined as it is also dependent on the vitamin D compound that is the subject of the treatment and is typically also determined in a clinical trial of efficacy for the vitamin D compound. In a preferred method of the invention utilizing